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A healthy peer status: Peer preference, not popularity, predicts lower systemic inflammation in adolescence

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ABSTRACT

In adolescence, sensitivity to peers is heightened, which makes peer experiences highly salient. Recent work suggests that these experiences may influence individuals' immune system functioning. Although there is a need to investigate which types of developmental salient social experiences affect inflammation, no studies have examined the role of peer status in inflammatory activity so far. This study is the first to examine the unique role of different types of peer status (i.e., peer preference and peer popularity) on systemic inflammation in adolescence, and the extent to which this association is moderated by early childhood adversity. Participants were 587 Dutch adolescents from the TRacking Adolescents´ Individual Lives Survey (TRAILS). Data were collected when participants were 11 (*SD* = .56), 13 (*SD* = .53) and 16 (*SD* = .71) years old, respectively. At age 11, early childhood adversity (e.g., hospitalization, death within the family) between 0–5 years was assessed via parent interviews. At age 13, peer preference and peer popularity were assessed with peer nominations of classmates. At age 16, high sensitive C-reactive protein (hsCRP), a marker of low-grade systemic inflammation, was assessed with a venipuncture blood draw. Results showed that adolescents who were rated low on peer preference at age 13 exhibited higher levels of hsCRP at age 16. Importantly, these effects remained after controlling for several covariates, including age, sex, peer victimization, smoking behavior, SES, fat percentage, physical activity and temperament. Additionally, we found a positive effect of peer popularity on hsCRP that depended on early childhood adversity exposure. This suggests that for those adolescents who experienced little early childhood adversity, high levels of peer popularity were associated with high levels of hsCRP. Overall, these findings suggest that it is important to take into account the independent roles of peer preference and peer popularity, as specific types of peer status, to better understand adolescent systemic inflammation.

1. Introduction

Adolescents spend much of their day interacting with peers and for most of them, being accepted and liked by peers is of chief concern (Somerville, 2013). In adolescence, peer sensitivity is heightened in comparison to other periods in life. Thus, not surprisingly, adolescents' social position in their peer group has a major impact on their psychological well-being and development (Parker and Asher, 1987; Prinstein and Giletta, 2016). Despite extensive attention to the consequences of peer status, researchers have rarely considered the extent to which these peer experiences may have consequences that extend beyond adolescent psychosocial well-being. Theoretical and empirical work suggests that social experiences may affect individuals' immune system activity (Slavich and Cole, 2013). However, the field has yet to identify specific developmentally salient stressors that can affect immune system functioning. The current study therefore set out to examine peer status antecedents of adolescent inflammation.

Inflammation, a key process of the immune system, is considered a pathway to many of the most common mental and physical health problems. Markers of systemic inflammation (e.g., C-reactive protein [CRP], a protein of the acute inflammation phase) are independent predictors of cardiovascular diseases, diabetes, and depressive symptoms (Valkanova et al., 2013). Recent research suggests that inflammatory activity is not only influenced by physical threats but can also be regulated by social factors. Because of the social nature of human beings, the immune system may have evolved to respond to experiences of social disconnection, given that in these situations physical injuries and infections are more likely to occur (Eisenberger

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et al., 2017; Slavich and Cole, 2013). Consistent with this possibility, environments that threaten the individual's social connections can increase inflammatory activity by up-regulating the expression of pro-inflammatory genes and down-regulating the expression of anti-viral genes, a process that has been referred to as Conserved Transcriptional Response to Adversity (CTRA; Slavich and Cole, 2013). Prolonged activation of pro-inflammatory pathways may eventually lead to elevated levels of systemic inflammation and therefore pose a risk for individuals' health. Indeed, broad measures of social experiences, including social rejection, social conflict, and social disconnection, have been associated with higher inflammation levels in adults as well as adolescents (e.g., Murphy et al., 2013; Allen et al., 2017). Conversely, experiences of social acceptance have been associated with lower levels of inflammation (Bajaj et al., 2016). Despite this evidence, however, no prior study has investigated whether different types of peer status may affect inflammation.

1.1. Peer status and inflammation

Two distinct forms of peer status have been identified in the developmental psychology literature, namely peer preference and peer popularity (Cillessen and Marks, 2011). Whereas peer preference is a combination of who peers like most minus who they like least (it is thus akin to likeability), peer popularity reflects the reputation of having social power (e.g., power to exert influence), access to resources, and visibility within the peer group (Prinstein et al., 2018). Research has indicated that adolescents distinguish between these two forms of peer status, and that both forms of status have different psychosocial correlates (LaFontana and Cillessen, 2002; Prinstein et al., 2018). For instance, peer preference has been associated with more prosocial behavior, less friendship conflict, higher ratings of perceived trustworthiness, and lower risk for developing both externalizing and internalizing problems (Litwack et al., 2012; Parkhurst and Hopmeyer, 1998; Prinstein et al., 2018). In contrast, peer popularity has been associated with higher levels of aggression, delinquency, and engagement in (health) risk behaviors (e.g., substance use; Cillessen and Mayeux, 2004; Choukas-Bradley et al., 2015). Furthermore, popular and well-liked adolescents show little overlap (Parkhurst and Hopmeyer, 1998). For example, popular peers may not be well-liked because in some instances they tend to be mean to their classmates and make use of aggression to maintain their high status (e.g., Cillessen and Mayeux, 2004; Merten, 1997). Peer preference and peer popularity thus represent different indicators of peer status.

The lack of research examining the unique role of these two types of peer status on adolescent inflammation represents a missed opportunity for at least three reasons. First, relationships with peers become more salient in adolescence and it is particularly important for adolescents to have positive connections with their peer group (Hartup and Stevens, 1997). Second, because of adolescents' heightened peer sensitivity, threats to social connections during adolescence may induce stronger emotional, neural and physiological responses than during other periods in life (Crone and Dahl, 2012; Somerville, 2013). Third, given the differences between the two types of peer status, it is important to examine their independent effects on systemic inflammation. Previous research has shown that broader experiences of acceptance and rejection that underlie peer preference may be relevant to inflammatory processes (Bajaj et al., 2016; Eisenberger et al., 2017; Slavich and Cole, 2013). However, it remains largely unknown whether peer popularity also predicts systemic inflammation, as no research has examined the constructs of peer popularity directly. Specifically, because peer popularity has also been associated with higher levels of stress exposure (Litwack et al., 2012), it remains unclear if low or high levels of peer popularity would be related to higher levels of inflammation (Murphy et al., 2013). This study aimed to fill this gap by investigating the independent associations of these two types of peer status with inflammation.

While investigating associations between peer status on inflammation, it is crucial to also take into account other more severe peer experiences that have been previously linked to inflammation. In this regard, prior studies have mostly focused on peer victimization. These studies revealed that peer victimization in childhood and adolescence is associated with higher levels of CRP in adulthood up to 30 years later and can predict steeper increases in CRP over time (Copeland et al., 2014; Takizawa et al., 2015). Although the two types of peer status and peer victimization show some overlap, previous research has indicated that they are only moderately correlated (Bukowski and Sippola, 2001). For example, low levels of peer preference can mean that adolescents are disliked or neglected but does not necessarily indicate that peers behave negatively towards them or have victimized them (Coie et al., 1982). Low levels of peer status most often indicate a weaker social position in the peer group that could pose a separate risk, in addition to victimization, for heightened inflammation. Indeed, psychoneuroimmunological research has suggested that disconnection and lack of integration may be sufficient to trigger inflammatory activity (Slavich and Cole, 2013). This study therefore examined whether peer preference and peer popularity predict inflammatory responses, even in the absence of less extreme and direct forms of peer threats.

1.2. The role of early childhood adversity

The effects of peer status on adolescent inflammation might be particularly strong for adolescents who have already experienced prior adversity. According to the stress-amplification and neuroimmune network model, adversities occurring in the first years of life may have long-lasting effects on immune system functioning by increasing individuals' reactivity to adversities occurring in subsequent periods (Miller et al., 2011; Nusslock and Miller, 2016; Rudolph and Flynn, 2007). Specifically, these adversities can increase the proinflammatory tendencies in monocytes and macrophages. The body sensitizes to the stressful environment early in life, and consequently may show more profound inflammatory responses when experiencing stressors later in life (Miller et al., 2011), such as during adolescence, when sensitivity to peer influences is theorized to be already heightened (Del Giudice et al., 2011). The stress-amplification model has been supported by findings that early life adversity may enhance inflammatory responses to stressors in adulthood (Carpenter et al., 2010; Kiecolt-Glaser et al., 2010; Pace et al., 2006). However, it has also been proposed that early adversity could affect responsivity to later stressors in the opposite way, by making individuals more resilient (see for instance, Seery et al., 2010). Overall, it is therefore unclear whether and how stressors occurring early in life and in adolescence interact to influence the immune system functioning.

1.3. The present study

In the present study, we aimed to extend existing research on social experiences and immune system functioning by examining for the first time the role of two different types of peer status (i.e., peer preference and peer popularity) among adolescents. Specifically, we had two aims: a) to investigate the independent ability of adolescent peer preference and peer popularity to predict systemic inflammation and b) to examine the moderating role of early childhood adversity on the link between the two types of peer status and systemic inflammation. To address these goals, we used data from TRAILS (TRacking Adolescents' Individual Lives Survey), a multi-informant longitudinal study that includes interview, self- and peer-reports, and blood samples to assay high-sensitivity CRP (hsCRP) from a large sample of adolescents. We hypothesized that peer preference at age 13 would be negatively related to hsCRP levels at age 16. However, because prior research has been inconsistent, no strong hypotheses on the direction of the association for peer popularity were formulated. Finally, we hypothesized that the associations between peer status and systemic inflammation would be

exacerbated by the experience of early childhood adversity. Specifically, we expected that low peer preference would more strongly predict higher hsCRP levels in adolescent with a history of early childhood adversity than in those without. Comparable to the main effect, no hypotheses were formulated for peer popularity. When examining these associations, we accounted for a number of possible confounding factors, including peer victimization, socio-demographic variables, health-related factors, and temperament. Gender differences were also explored, as initial evidence suggests that the association between social stress and systemic inflammation might be stronger in women than in men (Baldwin et al., 2018).

2. Material and methods

2.1. Participants and procedure

The sample consisted of 587 adolescents (54.6% females) from TRAILS, a multidisciplinary longitudinal study aimed at examining the social, mental and physical development of Dutch adolescents (De Winter et al., 2005). At baseline, adolescents were enrolled in the last two years of primary school (M_{age} = 11.11 years, SD = 0.56). The majority of the adolescents identified themselves as Dutch (92.6%), and had married parents (77.0%, divorced 13.8%, never married 8.2%, other 1.0%).

Participants were recruited on the basis of age (10–12 years old) from 122 primary schools from 5 selected municipalities in the north of the Netherlands. Next to assent from the child, the primary caregiver (e.g., parent or guardian) was asked to give consent for participation in the study. Of all targeted adolescents, 76.0% participated (for a more detailed description of the total TRAILS sample selection, sample characteristics, and methods, see De Winter et al., 2005). This resulted in a baseline sample of 2230 adolescents, who were followed until the age of 25 years for a total of 6 waves of data collection. The current study was based on data from the first three waves, when adolescents were approximately 11, 13 and 16 years old. At Wave 1, the response rate was 76.0%, and there were good retention rates at follow-up (96.4% at Wave 2; 81.6% at Wave 3).

At Wave 1, trained interviewers visited the parents or guardians at their home to administer a semi-structured interview. At Wave 2, a peer nomination procedure was administrated in all classrooms with at least three TRAILS participants, which was completed by participants as well as their classmates. Because of this, approximately 46.9% of the Wave 2 TRAILS participants (N = 1007) were included in the peer nomination procedure (see Fig. 1). Information about the consent procedure to recruit participants' classmates is presented in the Supplemental Information and a full description of the peer nomination procedure for

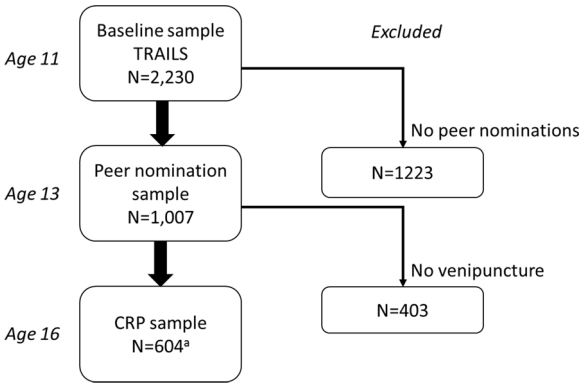

Fig. 1. Flowchart displaying the sample selection procedure. hsCRP = high-sensitivity C-reactive protein.
[a]An additional 17 participants with venipuncture were excluded because of abnormal hsCRP values (> 10; see description measures)

the TRAILS study can be found in Dijkstra, Lindenberg, and Veenstra (2008). At Wave 3, consent was obtained from participants and their parents for the collection of blood samples. From the adolescents who participated in the peer nomination procedure, 60.0% (N = 604) gave consent for the collection of blood samples (see Fig. 1). For this study, adolescents were selected who took part in both the peer nomination procedure and the collection of blood samples. Of those adolescents, 17 were excluded because of abnormal hsCRP values (see Measures section). We therefore ended up with a sample of 587 adolescents. These adolescents had significantly higher levels of SES and early childhood adversity than the excluded adolescents (N = 1643) from the baseline sample (see Table S1). No significant differences were observed on any of the other main study variables. The Central Committee on Research Involving Human Participants (the Dutch acronym being CCMO) approved the TRAILS study protocol at all three waves.

2.2. Measures

2.2.1. Early childhood adversity (age 0–5)

At Wave 1, information on major stressors occurring within the first five years of life was obtained with a standardized semi-structured parental interview administered by trained interviewers during the home visit. Based on previous studies (e.g., Bosch et al., 2012; Hughes et al., 2017; Slopen et al., 2015), six different adversities were selected to create a measure of early childhood adversity: child hospitalization, out-of-home placement, parental divorce, death of a family member, parental addiction, and other parental mental health problems. These adversities were chosen because they are the most commonly used in research examining early life adversity (for example, see Hughes et al., 2017). For most experiences, parents indicated whether the events occurred when the child was between 0 and 5 years old. For parental addiction and other mental health problems, parents indicated when in their lives they suffered from these problems. Each experience that occurred when the child was between 0 and 5 was counted, and a sum score was computed across all six adverse experiences, with higher values indicating more types of early childhood adversity (possible range 0–6; M = 1.03; SD = 1.20). Finally, the sum scores of childhood adversity were log transformed to normalize the data before analysis. Additional information about the semi-structured interview and validity of the measure can be found in the Supplemental Information.

2.2.2. Peer preference

At Wave 2, adolescents were asked to nominate an unlimited number of same- and cross-gender peers within their classroom whom they "like the most" and "like the least" (Coie and Dodge, 1983). To ensure anonymity, adolescents were provided with a roster including all classmates and were asked to report the numbers associated with the classmates they wished to nominate on a separate questionnaire. The nominations received by each participant on each criterion were summed and participants who received no nominations were included in the analyses with a total number of zero nominations. To account for differences in class size, received nominations were subsequently standardized to z-scores within classrooms and a peer preference score was computed by subtracting the standardized "liked least" nominations from the standardized "liked most" nominations. Finally, differences between the two standardized scores were standardized again within classrooms (M = 0.02; SD = 1.02; Coie and Dodge, 1983). This measure has been widely used and has proven reliable and valid (Cillessen, 2009).

2.2.3. Peer popularity

At Wave 2, peer popularity was assessed with the peer nomination item: "with whom do others want to associate?" (for a description of the peer nomination procedure see "Peer preference"). Peer popularity scores were then summed and standardized to z-scores within classrooms. This item explicitly disentangles personal preferences for being

associated with a person from reputation-based preferences by asking respondents to nominate people with whom others want to be connected. This measure of popularity has been previously used in other studies (see for example, Bowker et al., 2000) and showed convergent and discriminant validity with other types of peer status (see Dijkstra et al., 2008).

2.2.4. High-sensitivity C-reactive protein (hsCRP)

At Wave 3, blood samples were collected by a trained medical worker using venipuncture. Blood samples were drawn into serum separator tubes (5 ml with gel) and were collected at different locations, including schools, community centers or other research sites nearby participants' houses. Samples were transported to the laboratory within 4 h at room temperature. In the lab, the blood samples were centrifuged (10 min., 2500 g, 4C) and serum was stored at -80 degrees. Although blood centrifugation occurred later than what is typically recommended (120 min), pilot data and previous research have shown that using a 4 -h timeframe instead of the usual 2 -h one does not alter the results (Abraham et al. 2019; Tanner, Kent, Smith, Fletcher, & Lewer, 2008). Samples were analyzed within one week. hsCRP was determined using an immunonephelometric method, BN2, CardioPhase® hsCRP, Siemens, with a lower detection limit of 0.175 mg/L. Intra-assay coefficients of variation ranged from 2.1% to 4.4%, and inter-assay coefficients of variation ranged from 1.1% to 4.0%. Participants with hsCRP values higher than 10 mg/l were excluded from analyses ($N = 17$), as these values indicate acute infectious or inflammatory diseases that are unlikely to be related to the predictor variables examined in this study ($M = 0.94$; $SD = 1.44$) (Pearson et al., 2003). hsCRP values were log transformed to normalize the data before analysis.

2.2.5. Covariates

Peer victimization was assessed at Wave 2 with the peer nomination item "Whom do you bully?" (for a description of the peer nomination procedure see "Peer preference"). The proportion of nominations received by each adolescent as a victim of bullying was calculated. Due to the lack of variability and the extreme skewness of peer victimization, this variable was dummy coded to differentiate between victims and non-victims. Adolescents were classified as victims when they belonged to the top 10th percentile (Finkelhor et al., 2009).

Socio-demographic covariates included age, gender, SES, and ethnicity; all assessed at Wave 1.

Health-related covariates included current smoking behavior, fat percentage, contraceptive use, physical activity and medication use; all assessed at Wave 3.

Temperamental covariates included trait negative affect, extraversion, effortful control and affiliation, and were assessed at both Wave 1 and Wave 3. A detailed overview describing the measures used to assess all covariates can be found in the Supplemental Information.

2.3. Plan of analyses

First, bivariate correlations were conducted to examine associations among all study variables. To test the first two hypotheses, a series of hierarchical linear regression analyses were conducted with systemic inflammation (hsCRP) as an outcome. First (Step 1), we tested the effects of peer preference, peer popularity and early childhood adversity in an unadjusted model to account for possible suppression effects. In the subsequent steps, we added three types of covariates to test for robustness of the associations, starting with peer victimization and socio-demographic covariates (Step 2), followed by health-related covariates (Step 3) and temperamental covariates (Step 4). In Step 5, two separate models were run that included the interaction between early childhood adversity and either peer preference or peer popularity to test whether early childhood adversity moderated the association between peer status and systemic inflammation. Finally, additional linear regression analyses were conducted to explore gender differences by including 1) the interactions between gender and peer status and 2) a three-way interaction between gender, early childhood adversity and peer status. Gender differences were examined by adding interaction terms separately for peer preference and peer popularity. Significance levels were set at $p = < 0.0125$ to correct for multiple testing (four hypotheses; peer preference, peer popularity, and the two interactions with both types of peer status).

Missing data were observed only on the covariates (range 0–23.2%). Little's (1988) Missing Completely ad Random (MCAR) test was performed to assess the pattern of missing data. The Little MCAR test was significant, χ^2 (261) = 425.86, $p < .01$. However, the normed chi-square (χ^2/df = 1.61) justified the inclusion of adolescents with missing data in the analyses (Bollen, 1989). Thus, missing data were estimated using the expectation maximization (EM) algorithm.

3. Results

3.1. Descriptive analyses

Table S2 presents bivariate correlations among all study variables for descriptive purposes. A small negative correlation was observed between peer preference and hsCRP and a small positive correlation between peer popularity and hsCRP. Specifically, lower levels of peer preference but greater levels of peer popularity at age 13 were associated with higher levels of hsCRP at age 16. No significant correlation was found between early childhood adversity and hsCRP. Furthermore, hsCRP was positively correlated with negative affect and health-related covariates (i.e., smoking, fat percentage, anticonception use), and negatively with SES. Gender differences were observed in hsCRP and early childhood adversity, with females having higher hsCRP values, t (585) = 3.34, $p < .01$ (M = -.26 and -0.39, SD =.48 and 0.44 for females and males respectively), and males more early childhood adversity, t(585) = -4.83, $p < .01$ (M = 0.82 and 1.29, SD = 0.93 and 1.42, for females and males respectively).

3.2. Prediction of adolescent systemic inflammation at age 16

A small main effect of peer preference on hsCRP (see Table 1, Step 1) indicated that greater peer preference at age 13 predicted lower hsCRP levels at age 16. The significant association between peer preference and hsCRP held after adjusting for peer victimization, socio-demographic, health-related, and temperamental covariates (see Table 1, Steps 2–4). Conversely, however, a small positive effect of peer popularity on hsCRP (see Table 1, Step 1–2) suggested that greater levels of peer popularity at age 13 predicted *higher* hsCRP levels at age 16. However, the association between peer popularity and hsCRP was no longer significant when controlling for health-related and temperament covariates (see Table 1, Steps 3–4). No main effect of early childhood adversity on hsCRP was observed (see Table 1, Step 1).

In Step 5, no significant interaction effect between early childhood adversity and peer preference was found, b = 0.01; β = 0.02, 95% CI = [-0.05,.07], $p = .58$. This effect was almost identical in an unadjusted model without covariates, b =.01; β =.03, 95% CI = [--.05,.08], $p = .87$. However, a significant interaction effect between early adversity and peer popularity emerged, b = -.05; β = -.10, 95% CI = [-.08,-.01], $p < .01$, $R^2 = .25$, $\Delta R^2 = 0.01$. This effect was marginally significant in a model without covariates, b = -0.04; β = -0.09, 95% CI = [-0.08,-.01], $p = .02$. Specifically, peer popularity was positively associated with hsCRP for adolescents with low, but not average or high, levels of early childhood adversity (see Fig. 2).

3.3. Gender differences

Both the interaction terms of peer status with gender were not statistically significant; peer preference, b = 0.02, β = 0.04, 95% CI =

Table 1
Results from Hierarchical Regression Analyses Predicting hsCRP.

	Step 1			Step 2			Step 3			Step 4		
Steps and Predictors	*b*	95% CI R^2 = .02 F = 5.33**	β	*b*	95% CI R^2 = .08 ΔR^2 = .05***	β	*b*	95% CI R^2 = .24 ΔR^2 = .16***	β	*b*	95% CI R^2 = .24 ΔR^2 = .00	β
Step 1												
Early childhood adversity	−.01	[-.20,.12]	−.03	.00	[-.17,.15]	.00	.05	[-.10,.19]	.02	.04	[-.11,.18]	.02
Peer preference	−.06	[-.10,-.02]	−.13*	−.07	[-.10, -.02]	−.14*	−.06	[-.09, -.02]	−.12*	−.06	[-.09, -.02]	−.12*
Peer popularity	.04	[.01, .08]	.10+	.04	[.01,.08]	.10*	.03	[.00,.06]	.07	.03	[.00,.06]	.07
Step 2												
Age				.12	[.06,.18]	.16	.05	[.00,.11]	.07	.06	[.00,.11]	.07
Gender				−.14	[-.21, -.06]	−.15**	.17	[.08,.26]	.20**	.19	[.09,.29]	.20**
Ethnicity				−.03	[-.15,.14]	−.02	.00	[-.12,.15]	.01	.00	[-.12,.15]	.01
SES				−.05	[-.09,.00]	−.08+	.00	[-.04,.04]	.00	.00	[-.05,.05]	.00
Peer victimization				−.07	[-.19,.08]	−.04	−.10	[-.22,.02]	−.06	−.10	[-.22,.04]	−.06
Step 3												
Current smoking							.05	[-.02,.13]	.06	.06	[-.02,.15]	.06
Fat percentage							.03	[.02,.03]	.35**	.03	[.02,.04]	.31**
Contraceptive use							.42	[.30,.52]	.31**	.41	[.31,.53]	.34**
Physical activity							.04	[-.03,.11]	.04	.04	[-.04,.11]	.04
Medication use							.36	[-.04,.76]	.06	.34	[-.07,.74]	.06
Step 4												
Negative affect										.03	[-.02,.08]	.06
Extraversion										.00	[-.04,.06]	.02
Effortful control										.03	[-.03,.07]	.04
Affiliation										−.01	[-.05,.04]	−.02

Note., * $p < .0125$, ** $p < .001$. hsCRP = high sensitivity C-Reactive Protein. Step 5 was excluded from the table to limit complexity, as it provided little additional information.

[-0.05,.08], $p = .63$; peer popularity, b = -0.07, β = -.20, 95% CI = [-.17,.03], $p = 0.17$. This indicates that the effects of the two types of peer status on hsCRP did not differ between male and female adolescents. Both the three-way interactions between gender, peer preference and early childhood adversity and between gender, peer popularity and early childhood adversity were also not significant, b = -0.01, β = -0.03, 95% CI = [-0.08,.05], $p = .64$; b = .02, β = .05, 95% CI = [-.04,.09], $p = .51$, respectively. This suggested that the moderating role of early childhood adversity on the association between the two types of peer status and hsCRP was similar for males and females.

4. Discussion

Peer status (i.e., peer preference and peer popularity) is of high importance for adolescent development (Somerville, 2013), and has been associated with mental health outcomes (Parker and Asher, 1987; Prinstein and Giletta, 2016). Yet researchers have not explored whether different types of peer status predict adolescent levels of systemic inflammation over time. For peer preference, our results showed that adolescents with low levels of peer preference at age 13 exhibit higher levels of systemic inflammation (i.e., hsCRP) at age 16. These results were similar for females and males and remained significant after controlling for different types of confounding factors, including peer victimization, socio-demographics, health-related covariates and individual differences in temperament. Moreover, the association between peer preference and systemic inflammation was not moderated by early childhood adversity suggesting that peer preference predicts systemic inflammation equally for adolescents who experienced

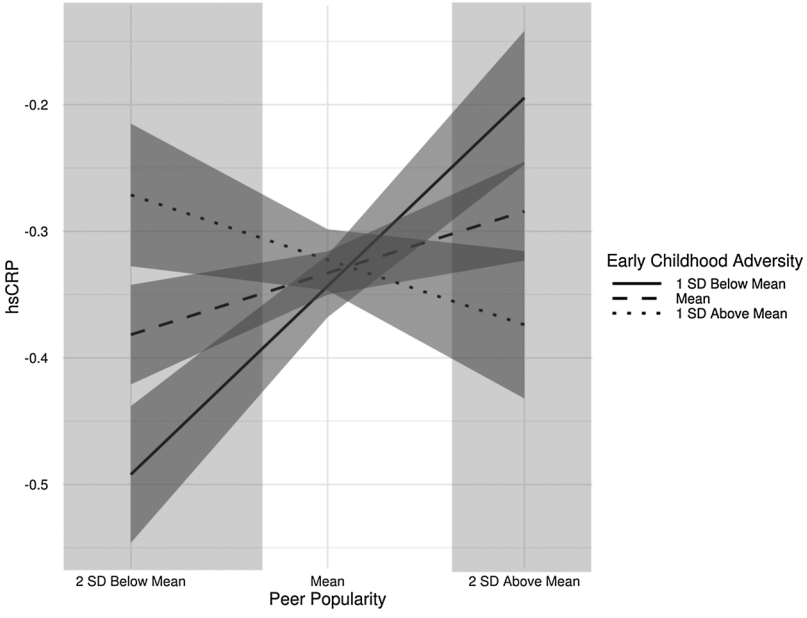

Fig. 2. Plot displaying the moderation of the association between Peer Popularity on levels of systemic inflammation by Early Childhood Adversity.
Note. hsCRP = log transformed high-sensitivity C-reactive protein; dark grey shaded areas- 95% Confidence Intervals; light grey shaded areas show area of significance (lower bound Z = -0.59; upper bound Z = 1.37). Only the simple slope of low levels of Early Childhood Adversity was significant (-1 SD, b = 0.07, $p < .01$; *M,* b = 0.02, $p = .17$; +1 SD, b = -0.03, $p = .34$).

different levels of adversity in early childhood. For peer popularity, however, our results showed that the association with inflammation depended on early childhood adversity. Specifically, among adolescents who had the least early childhood adversity, high levels of peer popularity were associated with the highest levels of hsCRP. Altogether, these results showed a small effect of peer status on adolescent systemic inflammation, which has important implications for future research.

The finding that low peer preference was associated with higher levels of systemic inflammation three years later suggests that, for adolescents, being accepted (and not rejected) by peers is not only important for their mental health but may also plays a role in their physical well-being. Although this effect was robust when adjusting for covariates and was comparable to prior studies (see for example, Baumeister et al., 2016; Copeland et al., 2014), it is important to acknowledge that it was small in size. Moreover, this effect was not moderated by early childhood adversity, which was in contrast with experimental studies showing that early life adversity can up-regulate acute inflammatory responses to social stressors later in life (Carpenter et al., 2010; Pace et al., 2006). Still, the association of peer preference with systemic inflammation extends prior work examining developmental outcomes associated with peer status (e.g., Parker and Asher, 1987; Prinstein and Giletta, 2016) and suggests that the consequences of low preference may be deeper than previously thought.

In addition to more extreme and direct forms of peer stress (e.g., peer victimization; see; Giletta et al., 2018; Takizawa et al., 2015), peer preference as a specific type of social connection was a noteworthy social factor for regulating immune system functioning in adolescence. This suggested that even low impact stressors, like low peer preference, can upregulate pro-inflammatory activity. This effect might stem from the evolutionary importance of being part of a group. Acceptance by group members increases chances of survival, while being rejected by the group makes individuals more vulnerable. Ultimately, the lack of social inclusion may trigger our bodies to prepare for harsher circumstances (Eisenberger et al., 2017). Thus, elevated levels of systemic inflammation because of poor peer connections could be seen as an evolutionary adaptive preserved response.

In contrast to peer preference, greater levels of peer popularity were associated with higher levels of systemic inflammation for those adolescents who had experienced little-to-no early childhood adversity. This suggests that high peer popularity may be stressful for some adolescents. For example, peer popularity has been associated with negative experiences, such as friendship conflict and aggression (Litwack et al., 2012; Cillessen and Mayeux, 2004), which may induce stress. Stress could also manifest because popular adolescents have more to lose, given their reputation and visibility within the peer group (Murphy et al., 2013). However, our results indicated that this stress only plays a role for adolescents who did not experience early childhood adversity. Contrary to our expectations, this moderation was not in line with a stress-amplification hypothesis but instead with an inoculation hypothesis. This hypothesis suggests that moderate levels of early childhood adversity may promote resilience and therefore can protect against negative outcomes later in life (Parker et al., 2006). Overall, this could explain why experiences of early childhood adversity might protect against the negative effects of peer popularity on systemic inflammation. Because we did not hypothesize this pattern, however, replication research is needed to substantiate this explanation.

The contrasting findings of peer preference and peer popularity highlight the importance of disentangling the two types of peer status (Prinstein et al., 2018). On the one hand, these findings suggest that being rejected, or not accepted, by the peer group may have stronger effects as compared to not being perceived as popular by the peer group. This could be due to the fact that while most adolescents are liked by their peers, only a few of them are really popular. Thus, lack of popularity is not necessarily a stressor and therefore may not represent a threat to social connections, as low peer preference does. There is also a difference in what greater levels of ratings within these two types of peer status entail. Whereas high ratings of peer preference are associated with positive outcomes, high ratings in peer popularity have a more mixed profile (Cillessen and Mayeux, 2004; Litwack et al., 2012; Murphy et al., 2013). These differences suggest the importance of looking at the independent effects of the two types of peer status in future research. Additionally, future research might also explore how these two types of peer status interact. A prior study revealed that youth who perceive themselves as having a greater social status also have more elevated inflammatory markers when they experience episodes of rejection (Murphy et al., 2013). Thus, low levels of peer preference may be particularly strong in upregulating inflammation for adolescents with high levels of popularity.

An additional noteworthy aspect of our findings was that peer ratings of social rejection (e.g., having fewer positive social ties) can influence adolescent systemic inflammation. Previous work has shown that self-reported and peer-reported experiences of social connection are at most only modestly correlated (Ledingham et al., 1982; Tucker et al., 2011), and it has been suggested that self-reported experiences (e.g., feelings of loneliness) might influence immune system activity more than less subjective experiences (e.g., number of friends; Slavich and Cole, 2013). Our results indicated that the less subjective (i.e., peer-reported) indicator of peer status—in particular peer preference—may increase inflammatory activity as well. This was consistent with a meta-analysis by Holt-Lunstad et al. (2015) that found no difference between the effects of subjective and objective experiences of social isolation on physical health.

In contrast to prior research, no association between early childhood adversity and systemic inflammation was found, even though substantial work has indicated that early life adversity predicts systemic inflammation in adolescence and later in life (e.g., Baumeister et al., 2016). Also within the TRAILS sample, trauma before the age of 16 was found to be related to inflammation (Jonker et al., 2017). It might be that the developmental period used to identify early childhood adversity in this study (0–5), which was purposely selected to disentangle the effects of earlier childhood experiences from those occurring later on during adolescence, is less relevant for predicting inflammation. While we included adversities between zero to up to five years of age, some other studies measured for a longer period, sometimes from zero to 12, 16 or even 18 years (Baumeister et al., 2016). A second reason for this null result might be due to differences in the experiences included in measures of early life adversity across studies (which can often go along with differences in age range). Unfortunately, in this study, no measure of verbal, physical and sexual abuse was available between ages zero to five. Additionally, the measure of early childhood adversity only had small variability as the present study consisted of a relatively healthy sample. Finally, it should be noted that retrospective recall is a limitation of this measure and that the questions, although based on validated measures widely used in prior studies (see for example, Caspi et al., 1996), had to be adjusted to be able to measure the age(s) at the time of adversity. Further research is necessary to examine how different types of stressors in different sensitive developmental periods interact to predict inflammatory activity.

In addition to the limitations related to the early childhood adversity measure, the insights from this study should be interpreted in light of other shortcomings. First, limitations related to the nature of the sample should be considered. This includes the limited ethnic diversity of the sample and the small number of victims in the sample. Specifically, the sample consisted mostly of adolescents self-identifying as ethnically Dutch, which makes it difficult to generalise the results to a more ethnically diverse population of youth. Additionally, although the sample size was adequate to test our hypotheses, only a small subset of adolescents (N = 58) were identified as victims. This limits the generalizability of the results. Second, although this research was longitudinal, it measured systemic inflammation only once, at the age of 16 years. Future research should additionally investigate changes in

systemic inflammation over time. This would also enable researchers to examine possible transactional effects and asses longer-term developmental consequences. Additionally, it is important for future research to examine other markers of inflammation, such as pro-inflammatory cytokines (e.g., interleukin-6 [IL-6], tumor necrosis factor alpha [TNF-α] or interleukin -1β [IL-1 β]). Future work should also assess other possible moderators, because not every adolescent reacts to the same extent to peer experiences (e.g., such differences could be related to levels of depression). Overall, given the small effect of peer preference on systemic inflammation, it is uncertain how relevant these effects are from a clinical perspective.

4.1. Conclusion

In sum, this study provided initial evidence of the importance of disentangling the roles of peer preference and peer popularity as specific types of social connections in order to further understand adolescent systemic inflammation. Consistent with and in addition to previous findings that extreme peer stressors can affect inflammation, we showed that peer preference is correlated with affect immune system functioning three years later in adolescence. This finding indicates a possible mechanism of how everyday peer experiences in adolescence can increase the risk of developing health problems later in life.

Declaration of Competing Interest

None.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.psyneuen.2019.104402.

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